IN THE CLAIMS

Please amend claims 8 and 12 as follows:

Claim 8, line 1, after "molecule" insert --from *Pasteurella haemolytica*--; and

Claim 12, line 2, delete "one or more".

REMARKS

Applicants have amended claims 8 and 12. Support for these amendments, if necessary, can be found throughout the specification. As no new matter is added by these amendments, as that phrase is defined under 37 C.F.R. § 1.118, their entry is respectfully requested.

The Examiner's comments in Office Action have been carefully considered. It is believed that the amended claims submitted herewith and the following remarks represent a complete response to the Examiner's rejections and place the application in condition for allowance. Reconsideration is respectfully requested.

Remarks Regarding Restriction Requirement

In the Office Action, restriction is deemed required under 35 U.S.C. § 121 to one of the following groups of claims:

Group I: Claims 1-4, 8, 10, 12, 14, 20 and 28, drawn to an isolated nucleic molecule encoding TbpA protein;

Group II: Claims 1, 5, 6, 7, 9, 11, 13, 15, 21 and 29, drawn to an isolated nucleic molecule encoding TbpB protein;

Group III: Claims 16 and 17, drawn to a purified and an isolated TbpA protein;

Group IV: Claims 18 and 19, drawn to a purified and an isolated TbpB protein;

Group V: Claim 22, drawn to an antibody of TbpA protein;

Group VI: Claim 22, drawn to an antibody of TbpB protein; and

Group VII: Claims 23-27, drawn to a vaccine comprising TbpA and TbpB.

Applicants elect Group I, claims 1-4, 8, 10, 12, 14, 20 and 28, with traverse.

As recited under M.P.E.P. 803, restriction is appropriate only when the groups can be shown to be distinct and there would be a serious burden placed on the Examiner to examine more than one group of claims. Such is not the case herein.

In the instant application, all of the claims relate to transferrin binding proteins of *Pasteurella haemolytica*. Accordingly, it would not be a serious searching burden to identify prior art that might fall into this one category. In view of this fact, it does not appear to place a serious burden on the Examiner to examine all claims together and it is requested that this requirement be withdrawn.

Remarks Regarding § 102

Claims 1-4, 8 and 10 stand rejected, under 35 U.S.C. § 102(b), as allegedly anticipated by Murphy et al. ("Murphy") (J. Clin. Microbiol. Sept. 1993, vol. 31, no. 9, 2303-2308). Applicants respectfully traverse this rejection.

Murphy is directed to the purification of total cell DNA from *Pasteurella haemolytica*. Murphy does not disclose or suggest a purified and isolated nucleic acid molecule encoding a transferrin binding protein. In addition, Murphy provides no guidance or suggestion to enable one of skill in the art to isolate a gene encoding a transferrin binding protein from the DNA crudely isolated from *Pasteurella haemolytica*. A product claim is not anticipated unless each element of the claimed product is disclosed in a single reference and the reference provides a method for making the claimed product. In re Donohue, 76 F.2d 531, 533, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985). As each and every element of the claims are not disclosed or suggested by Murphy, there can be no anticipation.

Thus, the rejection of claims 1-4, 8 and 10, under 35 U.S.C. § 102, is overcome and it is respectfully requested that it be withdrawn.

Remarks Regarding § 103

Claims 1-4, 8, 10, 12, 14, 20 and 28 stand rejected, under 35 U.S.C. § 103(a), as allegedly obvious over Murphy in view of Loosmore et al. ("Loosmore") (WO95/13370). Applicants respectfully traverse this rejection.

As discussed above, Murphy does not anticipate or render the claimed invention obvious because Murphy does not disclose or suggest the sequence or identification of a transferrin binding protein gene of *Pasteurella haemolytica*. The addition of Loosmore does not cure this deficiency. Loosmore is directed to nucleic acid molecules encoding a transferrin receptor from *Haemophilus influenzae*. Loosmore states at page 4, lines 32-35 that "the nucleic acid molecules provided herein are useful for the specific detection of strains of *Haemophilus*, and for the diagnosis of infection by *Haemophilus*" (underlining ours). There is nothing in Loosmore that would suggest or motivate one of ordinary skill in the art to obtain a nucleic acid sequence encoding a transferrin binding protein from *Pasteurella haemolytica* as recited in the claims of the present application.

However, it is alleged that it "is within the level of one of ordinary skill in the art to simply substitute routinely used procedures performed by Loosmore et al. for a transferrin binding protein from Haemophilus to another bacterial pathogen *Pasteurella haemolytica* of Murphy et al. because both the organisms share and/or expected to have sequence homology." Applicants respectfully disagree.

First, the procedures of Loosmore were not used to isolate the claimed sequences and, therefore, one cannot determine whether such would be successful. Second, the amino acid sequence encoded by the nucleic acid sequences of *Pasteurella haemolytica* only share 40% homology with the Haemophilus sequences described by Loosmore. Each of these points are addressed in greater detail below.

Methodology

Loosmore's method involves isolating membrane fractions from *Haemophilus influenza* and purifying proteins that bind transferrin from the membrane fractions using affinity chromatography on a column with immobilized transferrin. The proteins binding transferrin were isolated and used to prepare antisera in rabbits. The antisera was used to probe a chromosomal DNA library from *H. influenza*. Applicants used a different approach in isolating the nucleic acid molecules encoding the transferrin binding proteins. In particular, Applicants screened a *Pasteurella haemolytica* gene library using polymerase chain reaction (PCR) techniques. For the PCR, the Applicants prepared an oligonucleotide primer specific for the N-terminal amino acid sequence of the *Pasteurella haemolytica* TbpA protein that Applicants isolated and sequenced. An 0.8 Kbp DNA fragment was produced by PCR and used as a probe to screen the *Pasteurella haemolytica* library for a larger recombinant plasmid that contained the Tbp genes and subsequent walking by hybridization produced DNA over the entire Tbp genes. In contrast to the techniques described in Loosmore, antibodies were not used to isolate the TbpA gene.

Homology

Applicants did not use any of the sequence information provided in Loosmore to obtain their claimed nucleic acid molecules. In fact, although there is greater than 85% amino acid identity among the TbpA proteins from *Pasteurella haemolytica*, there is only 40% homology between the TbpA sequence of *Haemophilus influenza* and *Pasteurella haemolytica*. Consequently, due to the poor sequence identity between the genes from

Haemophilus influenza and *Pasteurella haemolytica*, the *Haemophilus* transferrin genes would not be useful as probes to isolate transferrin binding proteins from *Pasteurella haemolytica*. Consequently, had the inventors assumed that the *Pasteurella haemolytica* nucleic acid molecules encoding transferrin binding proteins would be highly homologous with the *Haemophilus influenza* nucleic acid molecules and used Loosmore's sequence as a probe, they would have been unable to isolate the claimed nucleic acid molecules. Hence, there is no indication that Murphy or Loosmore, alone or in combination, would suggest or enable the isolation of the claimed nucleic acid sequences.

Thus, as there is no suggestion found in the combination or a likelihood that a combination would succeed, the claimed invention cannot be considered obvious. The rejection of claims 1-4, 8, 10, 12, 14, 20 and 28, under 35 U.S.C. § 103, is overcome and should be withdrawn.

Remarks Regarding § 112, Second Paragraph

Claims 4, 8, 10, 12, 14, 20 and 28 stand rejected, under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Applicants respectfully traverse this rejection.

Specifically, the Examiner states that the terms "homologous" in claim 4, the phrase "stringent hybridization conditions" in claim 8, and the phrase "one or more" in claim 12 are indefinite. Applicants respectfully disagree. These terms and phrases are all well known and understood by those of skill in the art. In fact, such terms and phrases are commonly used in reference to nucleic acid sequences. Accordingly, no more is required

under § 112, second paragraph. Nevertheless, these terms and phrases are all defined in the specification. For example, the term "homologous" is described in the application on page 9, lines 13-21 and the phrase "stringent hybridization conditions" is defined in the application on page 9, lines 25-31. Although the phrase "one or more" is not indefinite, solely to expedite prosecution, this phrase has been deleted from claim 12.

Thus, the rejection of claims 4, 8, 10, 12, 14, 20 and 28, under 35 U.S.C. § 112, second paragraph, is overcome or moot and applicants respectfully request that it be withdrawn.

Remarks Regarding § 112, First Paragraph

Claims 1-4, 8, 10, 12, 14, 20, 28 stand rejected, under 35 U.S.C. § 112, first paragraph, as allegedly not enabling the claimed invention. Applicants respectfully traverse this rejection.

Specifically, while it is acknowledged that the specification is enabling for a TbpA of SEQ.ID.NO.:1 or SEQ.ID.NO.:2, it is alleged that the specification does not provide enablement for (a) sequences complimentary to, (b) sequences homologous to, or (c) a 15 base pair fragment of the TbpA of SEQ.ID.NO.:1. Applicants respectfully disagree.

As discussed in the specification, applicants were the first to isolate, clone and sequence a nucleic acid molecule encoding a transferrin binding protein from *Pasteurella haemolytica*. Claim 8 has been amended, without prejudice, to specify that the nucleic acid molecule is from *Pasteurella haemolytica*. All of the pending claims are specific for nucleic

acid sequences from *Pasteurella haemolytica* and applicant is not attempting to claim homologous sequences or fragments from other bacterial species. However, it would be unfair to request that the applicant limits their claims to the specific sequences disclosed in SEQ.ID.NO.:1 or SEQ.ID.NO.:2 as one of ordinary skill in the art having the benefit of the novel sequence provided in the patent application, could easily prepare sequences complementary to the nucleic acid sequence of SEQ.ID.NO.:1. In addition, one of ordinary skill in the art (again with the benefit of applicant's patent application), could prepare homologous variants and fragments of the nucleic acid sequence of SEQ.ID.NO.:1. Due to the degeneracy of the genetic code, one can make various known substitutions to the nucleotides of SEQ.ID.NO.:1 without affecting the amino acid sequence of the resulting protein. In addition, one can make various substitutions to the nucleic acid sequence that result in conservative amino acid substitutions in the resulting protein that do not affect the function or utility of the protein. Applicant has already inserted a numerical limitation on the degree of homology (80% homologous) and on the size of the fragments (at least 15 bases) in the claims. Applicant submits that the specification provides a sufficient written description to enable one of skill in the art to make and use the invention. No more is required under § 112, first paragraph.

In view of the foregoing, it is respectfully requested that the rejection of claims 1-4, 8, 10, 12, 14, 20 and 28, under 35 U.S.C. § 112, first paragraph, be withdrawn.

Conclusion

The application is in condition for allowance and the prompt issuance of a Notice of Allowance is respectfully requested. If there are any fees due with the filing of this response, including any additional fees due for a further extension of time, applicants respectfully Petition for that extension and request that any and all fees be charged to Deposit Account No. 02-0375.

Respectfully submitted,
BAKER & BOTTS, L.L.P.

Eric Sinn

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Eric Sinn
Registration No. 40,177

Enclosed: Check

Baker & Botts, L.L.P.
The Warner; Suite 1300
1299 Pennsylvania Ave., N.W.
Washington, D.C. 20004-2400
Tel: (202) 639-7700
Fax: (202) 639-7890